

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1(original). A targetable diagnostic and/or therapeutically active agent comprising a suspension in an aqueous carrier liquid of a reporter comprising gas-containing or gas-generating material, said agent being capable of forming at least two types of binding pairs with a target.

2(original). An agent as claimed in claim.1 wherein the gas comprises air, nitrogen, oxygen, carbon dioxide, hydrogen, an inert gas, a sulphur fluoride, selenium, hexafluoride, a low molecular weight hydrocarbon, a ketone, an ester, a halogenated low molecular weight hydrocarbon or a mixture of any of the foregoing.

3(original). An agent as claimed in claim 2 wherein the gas comprises a perfluorinated ketone, perfluorinated ether or perfluorocarbon.

4(original). An agent as claimed in claim 2 wherein the gas comprises sulphur hexafluoride or a perfluoropropane, perfluorobutane or perfluoropentane.

5(currently amended). An agent as claimed in claim 1 ~~any of the preceding claims~~ comprising gas microbubbles stabilised by a coalescence resistant surface membrane, a filmogenic protein, a polymer material, a non-polymeric and non-polymerisable wall-forming material or a surfactant.

6(original). An agent as claimed in claim 5 wherein said surfactant comprises at least one phospholipid.

7(original). An agent as claimed in claim 6 wherein at least 750 of the said surfactant material comprises phospholipid molecules individually bearing net overall charge.

8(original). An agent as claimed in claim 7 wherein at least 750 of the film-forming surfactant material comprises one or more phospholipids selected from phosphatidylserines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids and cardiolipins.

9(original). An agent as claimed in claim 8 wherein at least 800 of said phospholipids comprise phosphatidylserines.

10(currently amended). An agent as claimed in claim 1 ~~any of the preceding claims~~ wherein said gas-containing or gas-generating material is conjugated to at least two vectors or to one vector capable of binding to at least two binding sites.

11(currently amended). An agent as claimed in claim 1 ~~any of claims 1 to 9~~ wherein said gas-containing or gas-generating material is conjugated to one or more targeting vectors having specificity for one or more cellular surface receptors and further comprises moieties capable of binding to a receptor system so as to induce a therapeutic response.

12(currently amended). An agent as claimed in claim 1 ~~any of the preceding claims~~ wherein the vector or vectors are selected from antibodies; cell adhesion molecules; cell adhesion molecule receptors; cytokines; growth factors; peptide hormones and pieces thereof; non-bioactive binders of receptors for cell adhesion molecules, cytokines, growth factors and peptide hormones; oligonucleotides and modified oligonucleotides; DNA-binding drugs; protease substrates/inhibitors; molecules generated from combinatorial libraries; small bioactive molecules; and proteins and peptides which bind to cell-surface proteoglycans.

13(currently amended). An agent as claimed in claim 1 ~~any of the preceding claims~~ wherein the vector or vectors have affinity for targets at a level such that the agent interacts with but does not fixedly bind to said targets.

14(original). An agent as claimed in claim 13 wherein the vector or vectors are selected from ligands for cell adhesion proteins and cell adhesion proteins which have corresponding ligands on endothelial cell surfaces.

15(currently amended). An agent as claimed in claim 1 ~~any of the preceding claims~~ wherein the vector or vectors are sited such that they are not readily exposed to the target.

16(currently amended). An agent as claimed in claim 1 ~~any of the preceding claims~~ wherein the vector or vectors are coupled or linked to the reporter by means of avidin-biotin and/or streptavidin-biotin interactions.

17(currently amended). An agent as claimed in claim 1 ~~any one of claims 1 to 15~~ wherein the vector or vectors may be covalently or non-covalently coupled or linked to the reporter.

18(currently amended). An agent as claimed in claim 1 ~~any one of claims 1 to 15~~ wherein the vector is coupled or linked to the reporter by means of electrostatic charge interaction.

19(currently amended). An agent as claimed in claim 1 ~~any of the preceding claims~~ which further contains moieties which are radioactive or are effective as X-ray contrast agents, light imaging probes or spin labels.

20(currently amended). An agent as claimed in claim 1 ~~any preceding claim~~ further comprising a therapeutic compound.

21(original). An agent as claimed in claim 20 wherein said therapeutic compound is an antineoplastic agent, blood product, biological response modifier, antifungal agent, hormone or hormone analogue, vitamin, enzyme, antiallergic agent, tissue factor inhibitor, platelet inhibitor, coagulation protein target inhibitor, fibrin formation inhibitor, fibrinolysis promoter, antiangiogenic, circulatory drug, metabolic potentiator, antitubercular, antiviral, vasodilator, antibiotic, antiinflammatory, antiprotozoan, antirheumatic, narcotic, opiate, cardiac glycoside, neuromuscular blocker, sedative, local anaesthetic, general anaesthetic or genetic material.

22(currently amended). An agent as claimed in claim 20 ~~claims 20 or 21~~ wherein said therapeutic compound is covalently coupled or linked to the reporter through disulphide groups.

23(currently amended). An agent as claimed in claim 20 ~~or claim 21~~ wherein a lipophilic or lipophilically-derivatised therapeutic compound is linked to the reporter through hydrophobic interactions.

24(original). A combined formulation comprising:

- i) a first administrable composition comprising a pre-targeting vector having affinity for a selected target; and
- ii) a second administrable composition comprising an agent as claimed in any of the preceding claims, said agent comprising a vector having affinity for said pre-targeting vector.

25(original). A combined formulation as claimed in claim 24 wherein said pre-targeting vector comprises a monoclonal antibody.

26(currently amended). A combined formulation comprising:

- i) a first administrable composition comprising an agent an agent as claimed in claim 1 ~~any of claims 1 to 23~~, and

- ii) a second administrable composition comprising a substance capable of displacing or releasing said agent from its target.

27(original). A combined formulation comprising:

- i) a first administrable composition comprising an agent as claimed in claim 22, and
- ii) a second administrable composition comprising a reducing agent capable of reductively cleaving the disulphide groups coupling or linking the therapeutic compound and reporter in the agent of said first administrable composition.

28(original). A process for the preparation of a targetable diagnostic and/or therapeutically active agent as defined in claim 1 which comprises coupling or linking at least one vector to a reporter comprising gas-containing or gas-generating material: such that said agent is capable of forming at least two types of binding pairs with a target.

29(original). A process as claimed in claim 28 wherein a therapeutic compound is also combined with the reporter.

Claim 30(canceled).

31(currently amended). A method of generating enhanced images of a human or non-human animal body which comprises administering to said body an agent as claimed in claim 1 ~~any of claims 1 to 23~~ and generating an ultrasound, magnetic resonance, X-ray, radiographic or light image of at least a part of said body.

32(currently amended). A method as claimed in claim 31 which comprises the steps:

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- i) administering to said body a pre-targeting vector having affinity for a selected target; and thereafter
- ii) administering an agent ~~as claimed in any of claims 1 to 23~~, said agent comprising a vector having affinity for said pre-targeting vector.

33(original). A method as claimed in claim 32 wherein said pre-targeting vector comprises a monoclonal antibody.

34(currently amended). A method as claimed in claim 31 which comprises the steps:

- i) administering to said body an agent ~~as claimed in any of claims 1 to 23~~; and thereafter
- ii) administering a substance capable of displacing or releasing said agent from its target.

35(currently amended). A method as claimed in claim 31 ~~any of claims 31 to 34~~ wherein said agent further comprises a therapeutic compound.

36(original). A method as claimed in claim 35 wherein said therapeutic compound is covalently coupled or linked to the reporter through disulphide groups, and a composition comprising a reducing agent capable of reductively cleaving said disulphide groups is subsequently administered.

37(currently amended). A method for *in vitro* investigation of targeting by an agent as defined in claim 1 ~~any of claims 1 to 23~~ wherein cells expressing a target are fixedly positioned in a flow chamber, a suspension of said agent in a carrier liquid is passed through said chamber, and binding of said agent to said cells is examined.

38(original). A method as claimed in claim 37 wherein the flow rate of carrier liquid is controlled to simulate shear rates encountered *in vivo*.